

#### 09892613.ST25.txt SEQUENCE LISTING

<110> Shawn Shui-on

<120> REDUCING IMMUNOGENICITIES OF IMMUNOGLOBULINS BY FRAMEWORK-PATCHING

<130> 655

<140> US 09/892,613

<141> 2001-06-27

<160> 71

<170> PatentIn version 3.3

<210> 1

<211> 369

<212> DNA

<213> Artificial Sequence

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<223> FR-patched heavy chaim variable region sequence (Full DNA Sequence) formed by joining the N- and C- terminal (SEQ 3 and 6) halves at the KpeI site.

<220>

<221> V\_region

<222> (1)..(369)

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ccgggaaagg ggctggagtg ggtcgcatac attagtagtg gtggtggtac cacctactat 180
ccagacactg tgaagggccg attcaccatc tccagagaca atgccaagaa ctccctgtac 240
ctgcaaatga acagtctgag ggtggaggac acagccttat attactgtgc aagacatagt 300
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<211> 123 <212> PRT

<213> Chimaera sp.

<400> 2

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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser Ile Tyr 20 25 30

Asp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Page 1 40

Ala Tyr Ile Ser Ser Gly Gly Gly Thr Thr Tyr Tyr Pro Asp Thr Val 50 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr

Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Leu Tyr Tyr Cys

Ala Arg His Ser Gly Tyr Gly Ser Ser Tyr Gly Val Leu Phe Ala Tyr

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser 120

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N-template is a synthetic sense-strand oligonucleotide encoding amino acide 14-50 of the VH region (SEQ ID No. 2). The template is PCR-amplified by two primers (SEQ ID No. 4 and 5) <223>

<220>

<221> **V\_region** 

<222> (1)...(111)

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atgtcttggg ttcgccaggc accgggaaag gggctggagt gggtcgcata c 111

<210>

57 <211>

<212> DNA

<213> Artificial Sequence

<220>

<223> 5' Primer is a synthetic sense-strand oligonucleotide encoding amino acid 1-19 of the VH region (SEQ ID No. 2). The 3' end of the primer overlaps with the 5'end of the template by 18 nucleotides.

<220>

<221> primer\_bind
(1)..(57)

<222>

<400> 4

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57

60

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        DNA
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        Artificial Sequence
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         3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 43-59 of the VH region(SEQ ID No. 2). The
<223>
         primer overlaps with the template by 21 nucleotides.
<220>
         primer_bind
(1)..(48)
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                                                                                            48
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<213> Artificial Sequence
<220>
        C-terminal is a synthetic sense-strand oligonucleotide encoding
<223>
         amino acid 68-111 of the VH region (SEQ ID No 2) The template is PCR-amplified by two primers (SEQ ID No 7 and 8)
<220>
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         (1)..(132)
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gtggaggaca cagccttata ttactgtgca agacatagtg gctacggtag tagctacggg
                                                                                           132
gttttgtttg ct
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        Artificial Sequence
<213>
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        5' Primer is a synthetic sense-strand oligonucleotide encoding amino acid 55-74 of the VH region (SEQ ID No 2). The 3' end of the primer overlaps with the 5'end of the template by 21
<223>
         nucleotides.
<220>
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(1)..(60)
<221>
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ggtggtacca cctactatcc agacactgtg aagggccgat tcaccatctc cagagacaat
                                                                                            60
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<210> <211> <212> <213>	8 57 DNA Artificial Sequence
<220> <223>	3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 105-123 of the VH region (SEQ ID No 2). The primer and the template overlaps by 21 nucleotides.
<220> <221> <222>	primer_bind (1)(57)
	8 gaca gtgaccagag tcccttggcc ccagtaagca aacaaaaccc cgtagct 57
<210> <211> <212> <213>	9 321 DNA Artificial Sequence
<220> <223>	FR-patched light chaim variable region sequence formed by joining the N- and C- terminal (SEQ 11 and 14) halves at the KpeI site.
<220> <221> <222>	V_region (1)(321)
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ggtaag	gctc cgaaactcct gatctactac actagtatat tacactcagg agtcccatca 180
aggttc	agtg gcagtgggtc tggaacagaa tttactctca ccattagctc cctgcagcca 240
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ggcacc	aagg tggaaatcaa a 321
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Asp Ar	g Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr 20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Page 4 40

Tyr Tyr Thr Ser Ile Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro 65 70 75 80

Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp 85 90 95

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys 100 105

<210> 11

<211> 108

<212> DNA

<213> Artificial Sequence

<220>

N-template is a synthetic sense-strand oligonucleotide encoding amino acid 11-46 of the VL region (SEQ ID No. 10). The template is PCR-amplified by two primers (SEQ ID No. 12 and 13)

<220>

<221> V\_region

<222> (1)..(108)

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ctgtctgcct ctgtgggaga cagagtcacc attagttgca gggcaagtca ggacattagc

aattatttaa actggtatca gcagaaacca ggtaaggctc cgaaactc

60 108

<210> 12

<211> 51 <212> DNA

<213> Artificial Sequence

<220>

<220><223> 5' Primer is a synthetic sense-strand oligonucleotide encoding amino acid 1-17 of the VH region (SEQ ID No 10). The 3' end of the primer overlaps with the 5'end of the template by 21 nucleotides.

<220>

<221> primer\_bind

<222> (1)..(51)

<400> 12

gatatccaga tgacccagtc tccatcctcc ctgtctgcct ctgtgggaga c

51

<210> 13

<211> 40

<212> DNA

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<213> Artificial Sequence
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        3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 40-53. The primer and the template overlaps
<223>
        by 18 nucleotides.
<220>
        primer_bind
<221>
<222>
        (1)..(40)
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                                                                                40
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       120
<212> DNA
<213> Artificial Sequence
<220>
<223>
        C-terminal is a synthetic sense-strand oligonucleotide encoding
        amino acid 59-98 of the VH region (SEQ ID No 10) The template is
        PCR-amplified by tow primers (SEQ ID No 15 and 16)
<220>
<221>
        V_region
<222>
        (1)...(120)
<400> 14
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                                                                                60
cagccagaag attttgccac ttacttttgc caacagggta atacgcttcc gtggacgttc
                                                                               120
<210>
        15
<211>
       49
<212>
       DNA
<213>
       Artificial Sequence
<220>
<223>
        5' Primer is a synthetic sense-strand oligonucleotide encoding
       amino acid 50-65 of the VH region (SEQ ID No. 10). The 3' end of the primer overlaps with the 5'end of the template by 21
       nucleotides
<220>
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       primer_bind
<222>
       (1)..(49)
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ctacactagt atattacact caggagtccc atcaaggttc agtggcagt
                                                                                49
<210>
       16
<211>
       48
<212>
<213>
       Artificial Sequence
<220>
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#### 09892613.ST25.txt 3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 92-107 of the VH region (SEQ ID No 10). <223> The primer and the template overlaps by 21 nucleotides. <220> <221> primer\_bind <222> (1)..(48)<400> 16 48 tttgatttcc accttggtgc ctccaccgaa cgtccacgga agcgtatt <210> 17 371 <211> <212> DNA Artificial Sequence <213> <220> FR-patched heavy chaim variable region sequence (Full DNA <223> Sequence) formed by joining the N- and C- terminal (SEQ 19 and 22) halves at the KpeI site. <220> <221> **V\_region** <222> (1)..(371)<400> 17 60 caggtgcaac tggtggcttc cggggctgag gtaaataagc ctggggcctc agtgaaggtc tcctgcaagg cttctggcta cacatttacc agttacaata tgcactgggt acggcagcct 120 180 cctggaaggg gcctggaatg gattggagct atttatccag gaaatggtga tactagttac aatcagaaat tcaagggcaa ggccacattg actgcagaca aatcctccag cacagcctac 240 300 atgcagctca gcagtctgac atctgaggac tctgcggtct attactgtgc aagatcgcac 360 tacqqtaqta actacqtaga ctactttgac tactggggcc aaggcaccac tgttacagtc 371 tcctctgatc a <210> 18 <211> 123 <212> PRT <213> Chimaera sp. <400> 18 Gln Val Gln Leu Val Ala Ser Gly Ala Glu Val Asn Lys Pro Gly Ala

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr 20 25 30

Asn Met His Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile 40 45

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09892613.ST25.txt
Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe
Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr 65 70 75 80
Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
Ala Arg Ser His Tyr Gly Ser Asn Tyr Val Asp Tyr Phe Asp Tyr Trp
             100
                                   105
Gly Gln Gly Thr Thr Val Thr Val Ser Ser Asp
<210>
       19
<211>
       114
<212>
       DNA
<213>
       Artificial Sequence
<220>
       N-template is a synthetic sense-strand oligonucleotide encoding
<223>
       amino acide 12-49 of the VH region (SEQ ID No. 18). The template
       is PCR-amplified by two primers (SEQ ID No. 20 and 21)
<220>
<221>
<222>
       V_region
       (1)...(114)
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                                                                             60
                                                                            114
tacaatatgc actgggtacg gcagcctcct ggaaggggcc tggaatggat tgga
       20
<210>
<211>
       57
<212>
       DNA
<213>
       Artificial Sequence
<220>
<223>
       5' Primer is a synthetic sense-strand oligonucleotide encoding
       amino acid 1-19 of the VH region (SEQ ID No 18). The 3' end of the primer overlaps with the 5'end of the template by 24 ^{\circ}
       nucleotides.
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       primer_bind
<221>
<222>
       (1)..(57)
<400>
                                                                             57
caggtgcaac tggtggcttc cggggctgag gtaaataagc ctggggcctc agtgaag
<210>
       21
<211>
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<212> <213>	DNA Artificial Sequence
<220> <223>	3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 43-60 of the VH region (SEQ ID No 18). The primer and the template overlaps by 21 nucleotides.
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	21 tagt atcaccattt cctggataaa tagctccaat ccattccagg cccct 55
<210> <211> <212> <213>	22 126 DNA Artificial Sequence
<220> <223>	C-terminal is a synthetic sense-strand oligonucleotide encoding amino acid 70-111 of the VH region (SEQ ID No 18) The template is PCR-amplified by tow primers (SEQ ID No 23 and 24)
<220> <221> <222>	V_region (1)(126)
ttgact	22 gcag acaaatcctc cagcacagcc tacatgcagc tcagcagtct gacatctgag 60 gcgg tctattactg tgcaagatcg cactacggta gtaactacgt agactacttt 120
<210> <211> <212> <213>	23 61 DNA Artificial Sequence
<220> <223>	5' Primer is a synthetic sense-strand oligonucleotide encoding amino acid 57-76 of the VH region (SEQ ID No 18). The 3' end of the primer overlaps with the 5'end of the template by 21 nucleotides.
<220> <221> <222>	<pre>primer_bind (1)(61)</pre>
<400> tgatact	23 tagt tacaatcaga aattcaaggg caaggccaca ttgactgcag acaaatcctc 60
С	61

	09892613.S125.txt
<211> <212> <213>	59 DNA Artificial Sequence
<220> <223>	3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 105-123 of the VH region (SEQ ID No 18). The primer and the template overlaps by 21 nucleotides.
<220> <221> <222>	primer_bind (1)(59)
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<210> <211> <212> <213>	25 321 DNA Artificial Sequence
<220> <223>	FR-patched light chaim variable region sequence (Full DNA Sequence) formed by joining the N- and C- terminal (SEQ 27 and 30) halves at the BspEI site.
<220> <221> <222>	<pre>V_region (1)(321)</pre>
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tcctcc	ccca aaccctggat ttatgccaca tccaacctgg cttccggagt ccctagtcgc 180
ttcagt	ggca gtgggtctgg gaccgagttc actctcacaa tcagcagttt gcagcctgaa 240
gatttc	gcca cttatttctg ccatcagtgg agtagtaacc cgctcacgtt cggtgctggg 300
accaago	ctga ccgttctacg g 321
<210> <211> <212> <213>	26 107 PRT Chimaera sp.
<400>	26
Asp Ile 1	e Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly 5 10 15
Asp Arg	g Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met 20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr Page  $10\,$ 

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser

40

Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu 65 70 75 80

Asp Phe Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr 85 90 95

Phe Gly Ala Gly Thr Lys Leu Thr Val Leu Arg 100 105

<210> 27

<211> 129

<212> DNA

<213> Artificial Sequence

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N-template is a synthetic sense-strand oligonucleotide encoding amino acide 9-51 of the VL region (SEQ ID No. 26). The template is PCR-amplified by two primers (SEQ ID No. 28 and 29)

<220>

<221> V\_region <222> (1)..(129)

<400> 27

tcaagtcttt ctgcatctgt gggggacaga gtcacaatta cttgcagggc cagctcaagt 60 ttaagtttca tgcactggta ccagcagaag ccaggatcct cccccaaacc ctggatttat 120

gccacatcc

129

<210> 28 <211> 45

<212> DNA

<213> Artificial Sequence

<220>

<220><223> 5' Primer is a synthetic sense-strand oligonucleotide encoding amino acid 1-15 of the VH region (SEQ ID No 26). The 3' end of the primer overlaps with the 5'end of the template by 21 nucleotides.

<220>

<221> primer\_bind

<222> (1)..(45)

<400> 28

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45

<210> 29

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09892613.ST25.txt
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<211>
       40
<212>
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<213> Artificial Sequence
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        3' Primer is a synthetic anti-sense-strand oligonucleotide encoding amino acid 45-57. The primer and the template overlaps
<223>
        by 21 nucleotides.
<220>
        primer_bind
<221>
<222>
        (1)..(40)
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                                                                                  40
<210>
        30
        120
<211>
<212>
        DNA
<213> Artificial Sequence
<220>
        C-terminal is a synthetic sense-strand oligonucleotide encoding
<223>
        amino acid 61-100 of the VH region (SEQ ID No 26) The template is
        PCR-amplified by tow primers (SEQ ID No 31 and 32)
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        V_region (1)..(120)
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                                                                                120
<210>
        31
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        43
<212>
       DNA
<213>
       Artificial Sequence
<220>
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        5' Primer is a synthetic sense-strand oligonucleotide encoding
        amino acid 54-67 of the VH region (SEQ ID No 18). The 3' end of the primer overlaps with the 5'end of the template by 21 nucleotides.
<220>
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        primer_bind
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        (1)...(43)
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ggcttccgga gtccctagtc gcttcagtgg cagtgggtct ggg
                                                                                 43
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        32
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       42
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       DNA
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<220> 3' Primer is a synthetic anti-sense-strand oligonucleotide <223> encoding amino acid 94-107 of the VH region (SEQ ID No 26). primer and the template overlaps by 21 nucleotides. <220> <221> primer\_bind (1)..(42)<222> <400> 32 42 ccgtagaacg gtcagcttgg tcccagcacc gaacgtgagc gg <210> 33 <211> 123 <212> PRT Antibody <213> <400> 33 Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 10 15 Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Ala Phe Ser Ile Tyr  $20 \hspace{1cm} 25 \hspace{1cm} 30$ Asp Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu Glu Trp Val Ala Tyr Ile Ser Ser Gly Gly Gly Thr Thr Tyr Tyr Pro Asp Thr Val 50 60 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr 65 70 75 80 Leu Gln Met Ser Ser Leu Lys Ser Glu Asp Thr Ala Met Tyr Tyr Cys 85 90 95 Ala Arg His Ser Gly Tyr Gly Ser Ser Tyr Gly Val Leu Phe Ala Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ala <210> 34 <211> 107 <212> PRT <213> Antibody <400> 34 Asp Ile Gln Met Thr Gln Thr Thr Ser Ser Leu Ser Ala Ser Leu Gly Page 13

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr 20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile 35 40 45

Tyr Tyr Thr Ser Ile Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln 65 70 75 80

Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp 85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys 100 105

<210>

35 123 <211>

<213> Immunoglobulin

Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Ala Phe Ser Ile Tyr 20 25 30

Asp Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu Glu Trp Val
35 40 45

Ala Tyr Ile Ser Ser Gly Gly Gly Thr Thr Tyr Tyr Pro Asp Thr Val 50 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr 65 70 75 80

Leu Gln Met Ser Ser Leu Lys Ser Glu Asp Thr Ala Met Tyr Tyr Cys 85 90 95

Ala Arg His Ser Gly Tyr Gly Ser Ser Tyr Gly Val Leu Phe Ala Tyr 100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ala 115 120

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        Immunoglobulin
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        Immunoglobulin
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1 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser
20 25 30
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        38
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       30
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       PRT
        Immunoglobulin
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser 20 25 30
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       PRT
<213>
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       32
<212>
       PRT
<213>
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Met Asn Ser Leu Arg Val Glu Asp Thr Ala Leu Tyr Tyr Cys Ala Arg 20 25 30

<210> 41

<211> 11

<212> PRT

<213> Immunoglobulin

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<210> 42

<211> 107

<212> PRT

<213> Immunoglobulin

<400> 42

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1 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr 20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Asp Gly Thr Val Lys Leu Leu Ile  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Tyr Tyr Thr Ser Ile Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 60

Ser Gly Ser Gly Thr Asp Tyr Ser Leu Thr Ile Ser Asn Leu Glu Gln 65 70 75 80

Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp 85 90 95

Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys 100 105

<210> 43

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<212> PRT

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<400> 43

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09892613.ST25.txt
Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
Asp Arg Val Thr Ile Ser Cys
              20
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        Immunglobulin
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      44
Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile Tyr
<210>
        45
        32
<211>
        PRT
<212>
        Immunoglobulin
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Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Phe Cys 20 25 30
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<211>
        10
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        PRT
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Phe Gly Gly Gly Thr Lys Val Glu Ile Lys
1 5 10
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<210>
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        123
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Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly Gly
1 10 15
Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Phe Ser Ile Tyr 20 25 30
Asp Met Ser Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 35 40 45
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Ala Tyr Ile Ser Ser Gly Gly Gly Thr Thr Tyr Tyr Pro Asp Thr Val 50 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Val Glu Asp Thr Ala Leu Tyr Tyr Cys 85 90 95

Ala Arg His Ser Gly Tyr Gly Ser Ser Tyr Gly Val Leu Phe Ala Tyr 100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser 115 120

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<213> Immunoglobulin

<400> 48

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly 1 5 10 15

Asp Arg Val Thr Ile Ser Cys Arg Ala Ser Gln Asp Ile Ser Asn Tyr 20 25 30

Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile  $35 \hspace{1cm} 40 \hspace{1cm} 45$ 

Tyr Tyr Thr Ser Ile Leu His Ser Gly Val Pro Ser Arg Phe Ser Gly 50 55 60

Ser Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro 65 70 75 80

Glu Asp Phe Ala Thr Tyr Phe Cys Gln Gln Gly Asn Thr Leu Pro Trp  $85 \hspace{1cm} 90 \hspace{1cm} 95$ 

Thr Phe Gly Gly Gly Thr Lys Val Glu Ile Lys 100 105

<210> 49

<211> 123

<212> PRT

<213> Immunoglobulin

<400> 49

O9892613.ST25.txt
Gln Val Gln Leu Arg Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala
1 5 10 15 Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr 20 25 30Asn Met His Trp Val Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Ile 35 40 45 Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe 50 60 Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr 65 70 75 80 Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys 85 90 95 Ala Arg Ser His Tyr Gly Ser Asn Tyr Val Asp Tyr Phe Asp Tyr Trp 100 105 110 Gly Gln Gly Thr Thr Leu Thr Val Ser Ser Asp 115 120 <210> 50 <211> 107 Immunoglobulin <213> <400> Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1 10 15 Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met  $20 \hspace{1cm} 25 \hspace{1cm} 30$ His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr 35 40 45 Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser 50 60

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr 85 90 95

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu 65 70 75 80

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg 100 105

<210>

51 123 <211>

<212> **PRT** 

<213> Immunoglobulin

<400> 51

Gln Val Gln Leu Arg Gln Pro Gly Ala Glu Leu Val Lys Pro Gly Ala 1 5 10 15

Ser Val Lys Met Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr 20 25 30

Asn Met His Trp Val Lys Gln Thr Pro Gly Gln Gly Leu Glu Trp Ile 35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe 50 60

Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr 65 70 75 80

Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys 85 90 95

Ala Arg Ser His Tyr Gly Ser Asn Tyr Val Asp Tyr Phe Asp Tyr Trp
100 105 110

Gly Gln Gly Thr Thr Leu Thr Val Ser Ser Asp 115 120

<210> 52

<211> 30

PRT

<213> Immunoglobulin

<400>

Gln Val Gln Leu Val Ala Ser Gly Ala Glu Val Asn Lys Pro Gly Ala 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr 20 25 30

<210> 53

14 <211>

<212> PRT

<213> Immunoglobulin <400> 53

Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile Gly  $1 \hspace{1cm} 5 \hspace{1cm} 10$ 

<210> 54

<211> 32

<212> PRT

<213> Immunoglobulin

<400> 54

Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr Met Glu
1 5 10 15

Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg 20 25 30

<210> 55

<211> 32

<212> PRT

<213> Immunoglobulin

<400> 55

Arg Ala Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu Asn  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Cys Cys Ala Arg 20 25 30

<210> 56

<211> 11

<212> PRT

<213> Immunoglobulin

<400> 56

Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser 1 5 10

<210> 57

<211> 107

<212> PRT

<213> Immunoglobulin

<400> 57

Gln Ile Val Leu Ser Gln Ser Pro Ala Ile Leu Ser Ala Ser Pro Gly
1 10 15

Glu Lys Val Thr Met Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met 20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr Page 21 40

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser 50 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Val Glu Ala Glu 65 70 75 80

Asp Ala Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr 85 90 95

Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys Arg 100 105

<210> 58

<211> 23

<212> PRT

<213> Immunglobulin

<400> 58

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Asp Arg Val Thr Ile Thr Cys
20

<210> 59

<211> 22

<212> PRT <213> Immunoglobulin

<400> 59

Asn Leu Met Leu Ile Gln Pro Pro Ser Val Ser Glu Ser Pro Gly Lys
5 10 15

Thr Val Thr Met Thr Cys 20

<210> 60

<211> 15

<212> PRT

<213> Immunoglobulin

<400> 60

Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Pro Val Ile Tyr  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

<210> 61

<211> 32

<212> PRT

<213> Immunoglobulin

<400> 61

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Glu Phe Thr  $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$ 

Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Phe Cys 20 25 30

<210> 62

<211> 32

<212> PRT

<213> Immunoglobulin

<400> 62

Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr 1 10 15

Leu Thr Ile Thr Ser Leu Gln Pro Glu Asp Phe Ala Ala Tyr Phe Cys 20 25 30

<210> 63

<211> 32

<212> PRT

<213> Immunoglobulin

<400> 63

Gly Val Pro Ser Arg Phe Thr Gly Ser Gly Ser Gly Thr Asp Phe Phe 1 5 10 15

Leu Thr Ile Ser Ser Leu Arg Pro Glu Asp Val Ala Thr Tyr Phe Cys 20 25 30

<210> 64

<211> 32

<212> PRT

<213> Immunoglobulin

<400> 64

Gly Val Pro Ala Arg Phe Ser Gly Tyr Asn Ser Gly Asn Ser Ala Phe
1 10 15

Leu Thr Ile Asn Arg Val Glu Ala Gly Asp Glu Ala Asp Tyr Phe Cys 20 25 30

<210> 65

<211> 11

<212> PRT

<213> Immunoglobulin

<400> 65

09892613.ST25.txt Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg
1 5 10 <210> 66 <211> 11 <212> PRT Immunoglobulin <213> <400> Phe Gly Val Gly Ser Lys Val Glu Ser Lys Arg
1 10 <210> 67 <211> 11 <212> PRT <213> Immunoglobulin <400> Phe Gly Ala Gly Thr Lys Leu Thr Val Leu Arg
1 5 10 <210> 122 <211> <212> PRT <213> Immunoglobulin <400> 68 Gln Val Gln Leu Val Ala Ser Gly Ala Glu Val Asn Lys Pro Gly Ala 1 5 10 15 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr 20 25 30 Asn Met His Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile 35 40 45 Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe 50 60 Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr 65 70 75 80 Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys 85 90 95

Ala Arg Ser His Tyr Gly Ser Asn Tyr Val Asp Tyr Phe Asp Tyr Trp  $100 \hspace{1cm} 105 \hspace{1cm} 110$ 

Gly Gln Gly Thr Thr Val Thr Val Ser Ser

120

<210> 69

<211> 107 <212> PRT

<212> PRT <213> Immunoglobulin

<400> 69

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly 1 5 10

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met 20 25 30

His Trp Tyr Gln Gln Lys Pro Gly Ser Ser Pro Lys Pro Trp Ile Tyr 35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser 50 60

Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu 65 70 75 80

Asp Phe Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr 85 90 95

Phe Gly Ala Gly Thr Lys Leu Thr Val Leu Arg 100 105

<210> 70

<211> 122

<212> PRT

<213> Immunglobulin

<400> 70

Gln Val Gln Leu Val Ala Ser Gly Ala Glu Val Asn Lys Pro Gly Ala 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr 20 25 30

Asn Met His Trp Val Arg Gln Pro Pro Gly Arg Gly Leu Glu Trp Ile 35 40 45

Gly Ala Ile Tyr Pro Gly Asn Gly Asp Thr Ser Tyr Asn Gln Lys Phe 50 60

Lys Gly Arg Val Thr Ile Thr Ala Asp Lys Ser Thr Ser Thr Ala Tyr 65 70 75 80 Page 25

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys 85 90 95

Ala Arg Ser His Tyr Gly Ser Asn Tyr Val Asp Tyr Phe Asp Tyr Trp 100 105 110

Gly Gln Gly Thr Thr Val Thr Val Ser Ser 115 120

<210> <211> 107

<212> **PRT** 

Immunoglobulin <213>

<400> 71

Asp Ile Gln Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 10 15

Asp Arg Val Thr Ile Thr Cys Arg Ala Ser Ser Ser Leu Ser Phe Met  $20 \hspace{1cm} 25 \hspace{1cm} 30$ 

His Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Val Pro Val Ile Tyr 35 40 45

Ala Thr Ser Asn Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser 50 60

Gly Ser Gly Thr Glu Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu 65 70 75 80

Asp Phe Ala Thr Tyr Phe Cys His Gln Trp Ser Ser Asn Pro Leu Thr 85 90 95

Phe Gly Ala Gly Thr Lys Leu Thr Val Leu Arg 100 105